AMENDMENT

This is in response to the Office Action dated March 24, 2004 rejecting claims 1-4 and 6-36. Independent claims 1, 18 and 19 are amended herein. Claims 1-4 and 6-36 are pending.

Rejection Under 35 U.S.C. 112

The Examiner rejects claims 1-4, 6-18, and 20-33 under 35 USC 112, first paragraph, asserting that "applicant is now claiming a lipophilic liquid, camptothecin, at least one membrane-forming lipid, and an outer layer made of phospholipids." [Office Action, p. 2.]

Independent claims 1, 18 and 19 are herein amended to describe alternative embodiments of the invention as intended to avoid further misunderstanding of the claimed compositions. It should be further noted that other claims presented earlier in the prosecution of this application and its related cases are believed to be allowable over the references cited by the Examiner, which were in fact identified by Applicants themselves throughout the specification. Claims were amended earlier in an attempt to allow the Examiner to further appreciate the full scope of the claimed invention. Accordingly, reconsideration and allowance of all pending claims as presented now before the Examiner is respectfully requested.

Rejection Under 35 U.S.C. 103:

Claims 1-4 and 6-36 are rejected under 35 U.S.C. 103(a) based on Haynes (US 4725442) in view of Burke (US 5552156).

The Examiner explains in view of Burke that "the lactone ring of the camptothecin membrane bound drug is removed from the aqueous environment inside and outside of the liposome and is protected from hydrolysis, preserving the activity of the drug. Further, Burke teaches reducing the internal pH of the liposome to prevent hydroloysis of certain camptothecin drugs. See column 3, line 59 to column 4, line 2. Thus the lipid encapsulation creates an internal environment with a low pH to prevent hydrolysis of camptothecin drugs. (Note abstract)." [Office Action, p. 4.] Furthermore, the Examiner believed that "one would

be motivated to utilize the instant pH of both the internal liposome's aqueous phase and the external phase to prevent hydrolysis of camptothecin's lactone ring." [Id. at p. 5.] "Although Burke speaks to pH reduction mainly in the internal liposome compartment, the prior art clearly recognizes the problem of hydrolysis of camptothecin drugs in aqueous environments both on the *outside* and *inside* of the liposome. See column 3, lines 59-62. Thus, can apply this teaching to reduction of the pH both in and outside the liposome." [Id. at p. 6.]

The presented logic and arguments advanced the Examiner are circular. The purported impetus for the invention behind Burke was to protect camptothecin from an aqueous external environment such as blood plasma. ["camptothecin drugs are extremely susceptible to hydrolysis; in an aqueous environment such as blood plasma, the half life is about 16 to 29 minutes," column 1, lines 42 to 44.] So the lipid bilayer membrane space and internal compartment of the liposome thus provide protection from an external aqueous environment according to Burke that would hydrolyze the camptothecin lactone ring. [See Summary of Invention.] The idea of providing an external surrounding with a reduced pH outside of a liposome, e.g., suspension or carrier solution, is not expressed or suggested in Burke since that would obviate or eliminate an initial reason for protecting the camptothecin in the first place – namely removing or shielding it from the external environment with a liposome. It would therefore not be obvious to provide a microdroplet suspension or carrier solution with a reduced pH as claimed herein which further adds to the stability and activity of intravenous delivery of the claimed compositions.

Independent claims 1, 18 and 19 as amended herein are directed to injectable pharmaceutical compositions that include an aqueous microdroplet suspension or carrier solution having a pH less than 6.5. Accordingly, compositions with these and other limitations recited in the pending claims are neither suggested nor disclosed in the references cited by the Examiner.

Reconsideration and allowance of pending claims 1, 18 and 19 including all claims dependent thereon is respectfully requested.

CONCLUSION

It is submitted that the present application is in form for allowance, and such action is respectfully requested. Should the Examiner have any questions, please contact the undersigned attorney.

The Commissioner is authorized to charge any additional fees which may be required, including petition fees and extension of time fees, to Deposit Account No. 23-2415 (Docket No. 12636-898).

Respectfully submitted,

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